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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,502	09/13/2004	Yasuhiro Nishitani	067242-0174	6365

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EXAMINER	
BERCH, MARK L	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,502	NISHITANI ET AL.	
	Examiner	Art Unit	
	/Mark L. Berch/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/22/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,8-16,18 and 22-26* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,8-16,18,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 6, 8-10, 15, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura, 4788185, WO 97/41128, 4427677.

The reference disclosures were discussed previously. The references teach a chain with either zero or two methyl groups attached; applicants have exactly one. The compounds are thus homologs.

Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a prima facie case of obviousness of a compound may rest." The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ

247; *Ex parte Henkel,* 130 USPQ 474; *In re Jones,* 74 USPQ 152, 154; *In re Herr,* 134 USPQ 176; *Ex parte Dibella,* 157 USPQ 59; *In re Zickendraht,* 138 USPQ 22; *Ex Parte Fischer,* 96 USPQ 345; *In re Fauque,* 121 USPQ 425; *In re Druey,* 138 USPQ 39; *In re Bowers and Orr,* 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. As was stated directly in THE GENERAL TIRE & RUBBER COMPANY v. JEFFERSON CHEMICAL COMPANY, INC., 182 USPQ 70 (1974): "If any structural change is obvious to one skilled in the art, a substitution of the next higher homolog would seem to be." Note also *In re Jones,* 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge,* 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

In addition, 4788185, examples 84 and 85 teach the monomethyl, and the monoethyl substituents respectively, further rendering such choices obvious.

The declaration is unpersuasive. Declarant states, "Compound A demonstrated MIC that is lower or the same as MICs of both corresponding compounds B and C, i.e. compounds B and C from the same series, in 125 out of the 134 cases." But this lumps together unlike items. Legally speaking, situations where the MIC is the same is evidence that there is not unexpected effect. Situations where A is lower is potential evidence that there is an unexpected difference.

A comparison between A and B shows the following:

I. A is not better than B: 71 (53%)

II. A is twice as good as B (one dilution): 44 (33%)

III. A is more than twice as good as B (more than one dilution): 19 (14%)

A comparison between A and C shows the following:

I. A is not better than C: 64 (48%)

II. A is twice as good as C (one dilution): 49 (37%)

III. A is more than twice as good as C (more than one dilution): 21 (16%)

As was noted at the interview, applicants must establish that a two-fold difference (a single dilution) is actually significant, in a biological and statistical sense. The declaration did not take up this issue. As a result, the II category does not qualify as evidence of unexpected difference.

Determination of unexpected effects entails looking at both differences and similarities. If there are "too many similarities and too few differences", then unexpected effects cannot be considered demonstrated, *Sterling Drug Inc. v. Brenner*, 150 USPQ 584. Similarly, *In re GRAF*, 145 USPQ 197 states, "the conclusion required under section 103

must be grounded on a weighing of all the facts." Cf. also *In re DE MONTMOLLIN AND RIAT*, 145 USPQ 416; *In re Nolan*, 193 USPQ 641.

In this case, A has been established as better than the non-methyl B in just 14% of the tests; A has been established as better than the di-methyl C in just 16% of the tests. In both cases, this is insufficient. The similarities so greatly outweigh the differences that the strong structural obviousness has not been overturned.

Claims 1, 2, 4, 6, 8-10, 15, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4788185.

In addition, example 84 renders these claims obvious. This has the methylene with one methyl attached in the A linker. In addition, for claims other than claim 9, example 85 has methylene with one ethyl attached in the A linker. These two examples lack only the halo on the thiazole. However, the reference teaches that the thiazole with and without the halo are alternatively useable. Note the first structure at column 19, line 53; R2 can be H or Hal as set forth at column 21, lines 12-15. Examples of halothiazoles are seen in 92, 108-112, 133.

Claims 1, 2, 4, 6, 8-10, 15, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4427677.

The rejection is similar; the reference teaches carboxyalkyl generally in its definition of R2.

The declaration is of no value for these two latter rejections. The difference here is the presence or absence of Chloro on the thiazole, and the declaration is directed to an entirely different difference. That is, the declaration provides no comparison between thiazoles with and without the chloro substituent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4, 6, 8-16, 18, 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The last two lines are unclear. As written, this is part of the Z definition, which makes no sense at all. Applicants presumably mean "or an ester thereof". The next part presumably means "or a compound in which the amino group on the thiazole at the 7-position is protected". Correction is needed if this is what is intended.

1. A protecting group (in the aminothiazole) against what? These are final products, so what is there to protect against? As there is no such thing as a universal protecting group, correct selection of a protecting group requires some knowledge of what is being protected against.
2. It is not clear what the definition of Z embraces. If there were an N-containing heterocyclic group, and a second non-heterocyclic N, and it was the second N which was the cation, would that be covered? If there were an N-containing heterocyclic group, and it was substituted by COOCa, a moiety which has a net charge of +1, would that

qualify? It would not seems that such groups were intended, but the current claim language is broad enough to cover such moieties.

3. Further, the scope of "group" is unclear. Group is open-ended. For example, the moieties listed in claim 7 all consist of attachment directly to the heterocycle. However, "group" would be broad enough to cover e.g. the first choice of claim 11, in which the indicated N is not attached directly to the methylene at the 3-position of cephalosporin, but via a linker of unknown structure. It would cover, in effect, any moiety of any structure, so long as, somewhere, there was a cationic N, and there was a N-containing hetero. It would be unclear what such structures would look like.
4. Claim 9 has the claim dependency deleted, but no new claim number appears in the first line.

Claims 1-9, 15, 19-20, 22-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

See point 2-3 above. Because of the unlimited nature of this substituent, it cannot be deemed enabled or even described. For example, the linker is not described, and the present wording would cover a compound with a linker.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

9/26/2007